Original Article

Physiology Section

Mental Stress Induced Changes in Autonomic Nervous Activity in Normotensive Offsprings of Hypertensive Parents

JNANESHWARA P. SHENOY, SHIVAKUMAR J., KANMANI T.L., SHAILAJA MOODITHAYA, AMRIT MIRAJKAR, PREETHI GANAPATHI PAI

ABSTRACT

Back ground: The genetic component is a major contributor in the pathogenesis of essential hypertension. Consequently the likelihood of acquiring hypertension in offspring of hypertensive parents has been estimated to be higher when compared to that of normotensive individuals. The current study is an attempt to identify the early markers for the development of hypertension in these individuals by assessing the autonomic nervous activity when subjected to mental stress.

Methodology: Two groups of thirty normotensive subjects matched for age, body mass index, and physical activity were recruited .The only differentiating factor between the two groups being the genetic predisposition to hypertension of one group. Blood pressure & electrocardiogram was recorded in both groups at rest and during mental stress. Power spectral analysis of heart rate variability was done.Statistical analyses were conducted by paired & unpaired t-test. A p value of < 0.05 was considered as statistically significant.

Results: A significant decrease in high frequency normalized (HFnu) in the offspring of hypertensive parents was observed at rest. During mental stress, an increase in heart rate, systolic and diastolic blood pressure was observed in both groups. Increase in low frequency normalized and decrease in HFnu in offsprings of normotensive parents and increase in LF/HF ratio in individual with hypertensive parents were observed. Difference in basal and mental stress value of heart rate and systolic pressure was significantly more and HFnu was less in offspring of hypertensives.

Conclusion: Impairment in parasympathetic activity at rest and sympathovagal imbalance during mental stress is observed in individuals with hypertensive parents. This implies high chances of developing hypertension in their later life. So an evaluation of autonomic nervous activity by simple procedures like heart rate variability analysis to all individuals with a family history of hypertension in early stages of their life would prove to be invaluable. Life style modification such as regular exercises, yoga etc. can be suggested to those individuals who are found to be at the risk of developing hypertension.

Key Words: Mental stress, Hypertension, Heart rate variability parasympathetic

KEY MESSAGE

- The two groups involved in the study are matched for age, BMI, and physical activity. The important factor that differs in both groups is the genetic predisposition of hypertension in the group containing offsprings of hypertensive parents.
- An impairment in parasympathetic activity in young offspring of hypertensives even at rest is found.
- Sympothovagal imbalance during mental stress is observed in individuals with hypertensive parents. This implies high chances of developing hypertension in their later life.
- An evaluation of autonomic nervous activity by simple non-invasive procedures like HRV analysis to all individuals with the family history of hypertension in early stages of their life can reveal the future risk of development of hypertension
- Life style modification such as regular exercises, Yoga etc. can be suggested to those individuals who are found to be at risk of developing hypertension.

INTRODUCTION

Hypertension is one of the major risk factors for coronary artery diseases, congestive heart failure, stroke, peripheral vascular disease, kidney failure and retinopathy. Essential hypertension is characterized by an increase in sympathetic nervous system activity, reduced vagal modulations of the sinoatrial node and blunted baroreflex gain. Since incidence of genetic component of essential hypertension is as high as 60%, normotensive offspring of one essential hypertensive parent are at increased likelihood to develop essential hypertension [1, 2]

Although the pathogenesis of essential hypertension is unclear, dysregulation of the autonomic nervous system with evidence of sympathetic hyperactivity and/or vagal withdrawal has been implicated in its development. Heart rate variability (HRV) has emerged as a practical, non-invasive tool to quantitatively investigate cardiac autonomic dysregulation in hypertension. Studies have reported a decreased HRV among hypertensive patients and that the relation between blood pressure and HRV is present across a wide range of blood pressure [3, 4].

HRV is an important indicator of both physiological resiliency and behavioral flexibility, reflecting the individual's capacity to adapt effectively to stress and environmental demands. It has become apparent that while a large degree of instability is detrimental to efficient physiological functioning, too little variation can also be pathological. An optimal level of variability within an organism is a key regulatory system which is critical to the inherent flexibility and adaptability that epitomize healthy function.

Various previous studies have shown that mental stress increases sympathetic activity and decreases parasympathetic activity [5, 6, 7]. This results in increased strain on the heart, immune and hormonal systems. Acute period of mental stress can also results in reduced HRV. This phenomenon suggests a mechanism through which psychological stress may exacerbate cardiac rhythm disturbances [8].

One of the most active areas in psychosomatic research has focused on cardiovascular reactivity to mental stress. The underlying assumption of this study is that excessive cardiovascular responses of stress plays a key role in the development of hypertension. The necessity of this study is further strengthened by the lack of extensive literature on the effect of mental stress on autonomic nervous activity in normotensive offspring of normotensive and hypertensive parents. Hence the present study is designed to evaluate the effect of mental stress on autonomic nervous activity between healthy normotensive offspring of normotensive parents as compared to that of hypertensive parents.

MATERIALS AND METHODS

A total of 60 healthy normotensive subjects aged between 18-25 years with a normal BMI and leading a sedentary life style were considered. Thirty subjects, having at least one hypertensive parent constituted the study group. The control group consisted of thirty age and sex matched individuals with normotensive parents. All the subjects were recruited from KS.Hegde Medical Academy campus at Deralakatte, Mangalore after a thorough clinical examination. Informed written consent was obtained from all the participants, and the experiment protocol was approved by the Institutional Ethics committee. Athletes, those who practice yoga or exercises, those with history of cardiovascular, respiratory, psychiatric diseases and consumption of alcohol and tobacco or any medications that affect the autonomic nervous activity were excluded. There were no dropouts in either the subject or control group that were recruited.

All the participants reported for the study, after refraining from food for at least 2 hours. They were also instructed not to consume caffeinated or cocoa containing beverages 12 hours prior to recording. Height was measured to the nearest 0.1cm without footwear using vertically movable scale. Weight was measured to the nearest 100 grams using a digital scale and BMI was calculated.

Prior to recording of the electrocardiogram (ECG), the subjects were required to take rest for a period of 15 minutes. A basal recording of blood pressure was taken using a mercury sphygmomanometer, with the subject in supine position. 3M standard chest electrodes (Ag- AgCl) were used and electrodes were placed on the right upper limb and both the lower limbs. A basal ECG recording for 5 minutes was taken with the subject in the supine position.

Mental stress test was performed using standard serial subtraction test [9]. A serial subtraction mathematical task was chosen as the stressor in this study because mental math was easy to administer and offers infinite variations and less ethical problems than other active stressors. ECG was recorded for a period of 5 minutes from the time he/she started the serial subtraction task (i.e. onset of mental stress). Immediately blood pressure was recorded in the same position.

It was ensured that the subjects were awake, supine and breathing normally, and they were asked to avoid unnecessary movements during this entire period.

HRV Analysis: A noise- free ECG was obtained with the sampling frequency of 1024 Hz. Spectral analysis was performed off-line using POWERLABS-(Version 7.0). Data was edited manually for artifacts. HRV software used a peak detection alogrithm to find the 'R' wave. The detection was done at a re-sampling rate of 4 Hz. Each detected 'R' wave was considered as a data point. A minimum of 256 data points are required to perform a spectral analysis, for which a minimum duration of 5 minutes of ECG recording was required.

Spectral analysis was performed using a Fast Fourier Transformation (FFT). The power was calculated in two bands: the 0.15-0.4 Hz band of RR power considered as high frequency (HF) reflects parasympathetic nerve activity to the heart, while 0.04-0.15 Hz considered as low frequency band (LF) was believed to reflect at least in part, sympathetic nervous activity to the heart. In addition to absolute power, the data was also presented as normalized units (HFnu & LFnu). The ratio of low frequency to high frequency (LF/ HF) represents a measure of the balance of sympathetic and parasympathetic function [10, 11].

Statistical Analysis: Total study population of sixty comprised of two independent groups containing thirty subjects each. Data was analyzed using independent t -test for comparison of HRV parameters, heart rate and blood pressure between the two groups. Paired t-test was used for comparison of same parameters obtained during rest and mental stress within the same group. Effect of mental stress was analyzed by comparing the differences between values recorded at rest and during mental stress between control and study group using unpaired t- test.

RESULTS

The anthropometric data showed no significant difference between the offspring of normotensive and hypertensive parents as depicted in [Table/Fig-1].

There was no significant difference between the control and the study group with respect to heart rate, systolic and diastolic blood pressures when measured at rest [Table/Fig-2]. However, high frequency normalized (HFnu), was significantly, lower in study group ($p<0.001$) [Table/Fig-3].

During mental stress both study as well as control group exhibited significant increase in heart rate, systolic and diastolic blood pressures [Table/Fig-2]. A significant increase in Lfnu and a decrease in HFnu were observed in the control group when compared to their basal values. There was a similar significant increase in LF/HF ratio in the study group when compared to its basal value [Table/Fig-4].

On comparing the mean values of the difference in various parameters, (heart rate, systolic and diastolic blood pressure and HRV)

Variables	Offspring of Normotensive parent	Offspring of Hypertensive parent
Age	20.46 ± 0.83	20.37 ± 1.40
Height	165.99+ 9.13	162.81 ± 7.67
Weight	57.54 ± 8.61	55.96 ± 7.36
BMI	20.78 ± 1.56	21.03 ± 1.46

[Table/Fig-1]: Anthropometric data
(Results are presented in Mean ± SD).

		Basal	Mental stress	Difference
Offspring of Normotensive parents (N=30)	Heart Rate (bpm)	72.98 ± 7.71	79.52 ± 8.30*	6.54 ± 3.33
	SBP (mm of hg)	113.93 ± 6.09	122.07 ± 7.06*	8.13 ± 5.43
	DBP (mm of hg)	71.4 ± 6.33	77.13 ± 6.33*	5.73 ± 5.48
Offspring of Hypertensive parents (N=30)	Heart Rate (bpm)	75.42 ± 8.75	84.21 ± 9.09*	8.79 ± 2.89**
	SBP (mm of hg)	113.8 ± 7.49	124.87 ± 6.15*	11.07 ± 3.67**
	DBP (mm of hg)	72.87 ± 8.39	79.33 ± 6.96*	6.47 ± 3.00

[Table/Fig-2]: Showing heart rate and blood pressure changes at rest and during mental stress.
(Results are presented in Mean ± SD . *p< 0.05, **p < 0.01).

Parameters	Offspring of Normotensive parents (N=30)	Offspring of Hypertensive parents (N=30)
Total power (ms^2)	9936.44 ± 3641.23	6199.23 ± 1188.93
Low Frequency (absolute in ms^2)	2473.04 ± 935.36	1386.83 ± 132.95
High Frequency (absolute in ms^2)	4400.23 ± 1821.95	1664.28 ± 182.87
Low Frequency (normalized)	33.73 ± 2.52	39.69 ± 2.67
High Frequency (normalized)	53.52 ± 2.91	41.26 ± 2.53**
LF/HF	0.88 ± 0.19	1.12 ± 0.14

[Table/Fig-3]: Showing HRV parameters at rest
(Results are presented in Mean ± SEM . *p< 0.05, **p < 0.01).

at rest and during mental stress, the change in heart rate and systolic blood pressure was found to be more in the study group [Table/Fig-2] Among the changes observed in HRV parameters as shown in the [Table/Fig-4] only difference in Hfnu was found to be significantly less in the study group (p<0.05).

DISCUSSION

The rhythmic beating of the heart at rest is believed to be monotonously regular; it is now known that the rhythm of a healthy heart under resting conditions is actually surprisingly irregular. These moment-to-moment variations in heart rate was easily overlooked when average heart rate is calculated. HRV derived from the ECG is a measurement of these naturally occurring, beat-to-beat variations in heart rate.

This non-invasive, detailed and sophisticated analysis of fluctuations in heart rate can be used to indirectly assess the autonomic control of heart. Changes in the HRV pattern provides an early and sensitive indicator of compromised health. A high variability in heart rate is a sign of good adaptability, implying a healthy individual with a well functioning autonomic control mechanism. Conversely, lower variability is often an indicator of abnormal and insufficient adaptability of the autonomic nervous system implying the presence of a physiological malfunction.

The present study is an attempt to assess and compare the autonomic nervous activity by analysis of HRV at rest and during mental stress on young normotensive offspring of normotensive and hypertensive parents divided in two separate groups. Since factors like age, obesity and physical activity can influence the HRV, we included only those individuals that match for these factors. On statistical analysis of the anthropometric data [Table/Fig-1] no significant difference was noted in age, height, weight and BMI.

An analysis of the HRV data obtained at resting state in both the groups [Table/Fig-1] revealed that there was a significant reduction in HFnu of the offspring of hypertensive parents. Similar findings were also observed by Soumya et al [12], Maver et al [13] and Wu J S et al [14]. HFnu was considered as an index of modulation of parasympathetic branch of autonomic nervous system (ANS) as it influenced the sinoatrial node. This was suggestive of an early onset of impairment of parasympathetic activity of autonomic nervous system at cardiac level in offspring of hypertensive individuals.

A significant increase in LFnu, average heart rate, systolic and diastolic blood pressure and a decrease in HFnu were observed in offspring of normotensive parents [Table/Fig-1 and 4]. The study

Variables	Offspring of Normotensive parents(N=30)			Offspring of Hypertensive parents(N=30)		
	Basal	Mental sterss	Difference	Basal	Mental stress	Difference
Total power (ms^2)	9936.44 ± 3641.23	9426.76 ± 3329.58	283.37 ± 3548.11	6199.23 ± 1188.93	6229.91 ± 1809.60	30.68 ± 1081.19
Low Frequency (absolute in ms^2)	2473.04 ± 935.36	2996.88 ± 1160.05	663.12 ± 1066.49	1386.83 ± 132.95	1695.53 ± 474.47	308.69 ± 455.56
High Frequency (absolute in ms^2)	4400.23 ± 821.95	3357.31 ± 1241.63	641.48 +1613.96	1664.28 ± 182.87	1508.3 ± 330.13	155.98 ± 306.13
Low Frequency (normalized)	33.73 ± 2.52	41.02 ± 2.98	7.477 ± 2.69	39.69 ± 2.67	42.2 ± 2.97	2.51 ± 2.51
High Frequency (normalized)	53.52 ± 2.91	44.89 ± 2.65	9.263 ± 6.23	41.26 ± 2.53*	40.54 ± 2.93	0.723333 ± 2.9394*
LF/HF	0.88 ± 0.19	1.16 ± 0.13	0.31433 ± 0.2017	1.12 ± 0.14	1.47 ± 0.22	0.346 ± 0.168628

[Table/Fig-3]: Showing the effect of mental Stress on HRV parameters in both groups
(Results are presented in Mean ± SEM . *p< 0.05, **p < 0.01).

conducted by Andrei et al [15] reported an increase in heart rate, mean arterial pressure and LFnu with a decrease in HFnu, when individuals were subjected to mental stress. LFnu is viewed as an indicator of aggregate modulation of both sympathetic & parasympathetic branches of ANS. Devrath et al [1] in a previous study have shown that an increase in LF & decrease in HF is suggestive of an overall increase in sympathetic activity leading to an increase in average heart rate and BP during mental stress in offspring of normotensive parents.

However, those with hypertensive parents showed a significant increase in LF/HF ratio, average heart rate, systolic and diastolic blood pressure [Table/Fig-4]. LF/HF ratio is a widely used HRV index of sympothovagal balance between the two branches of autonomic nervous system. Dayanand G et al [16], found an increase in heart rate, systolic and diastolic blood pressure similar to the present study but they noticed these findings during physical stress in offspring of hypertensives and suggested that in young normotensive subjects, parental hypertension was associated with stiffening of carotid artery and reduction in cardiovagal outflow and baroreflex gain. This dysregulation in autonomic nervous system can explain an increase in heart rate, systolic and diastolic blood pressure.

In the present study the difference in HFnu which was significantly less in offspring of hypertensive subjects when compared with the basal value was suggestive of reduced modulation of parasympathetic activity. It was also noted that the differences between basal and mental stress values of heart rate and systolic pressure were significantly higher, in those who had positive family history of hypertension. This may be due to a hyperactive sympathetic nervous system which may lead to further consequences like peripheral vasoconstriction, an increase in heart rate, resulting in increase in peripheral vascular resistance with rise in systemic blood pressure[17]. In support of this, Falkner B et al[18], noticed a rise in plasma catecholamine levels in association with increased sympathetic activity in individuals with genetic predisposition to hypertension. Noll G et al[19], in a similar study found that the activity of the sympathetic nervous system and plasma norepinephrine and endothelin levels are increased during mental stress in offspring of hypertensive parents. Endothelin was a locally released vascular regulator that at very low concentrations enhances constriction in the presence of norepinephrine and at higher concentrations had potent direct vasoconstrictor properties. These early functional changes of central and local cardiovascular regulation may be important in the pathogenesis of essential hypertension

The fact that the offspring of hypertensive parents were still normotensive indicates that the observed changes in cardiovascular responsiveness occur at an early stage, are probably of genetic origin, and could play a role in the pathogenesis of hypertension. Evidence of reduced parasympathetic modulation and elevated sympathetic activation at such an early stage of life in offspring of hypertensives suggest the necessity of targeting reduction in sympathetic activation as a primary goal in prevention of hypertension. This could be achieved by early identification of individual with 'pre-hypertensive' state and by implementing preventive measures like regular exercises change in food habits and life style modification such as Yoga.

CONCLUSION

HRV analysis brings to fore the subtle yet critically important changes in autonomic activity occurring during the normal beating of the heart. Analysis of these changes provides an important insight into the autonomic nervous system. This tool was therefore employed to scout for autonomic nervous system perturbations in normotensive individuals with a genetic susceptibility for hypertension. This study found that in these subjects there was a reduced modulation of para-sympathetic activity and a hyperactive sympathetic nervous system when subjected to mental stress. Since these subjects were essentially normotensive at rest, therefore these two features may constitute a "pre-hypertensive "state. Such findings in a young normotensive individual may serve as a "red flag" for future development of hypertension and thereby help them in adopting changes in diet and lifestyle in order to thwart the development of hypertension. Some of the limitations of our study which if covered by future studies would throw more light on the effect of stressors to uncover the "dormant" hypertension in genetically susceptible individuals are as follows. In our study we were not able to evaluate the beat-to-beat variations in BP and this could probably have provided a more complete picture about the autonomic control of entire cardiovascular system. Further our study included only offspring's of parents wherein only one parent was hypertensive, whether having both parents who are hypertensive further adds to the changes observed has to be studied. Finally whether addition of other stressors accentuates the observed changes also needs to be evaluated.

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AUTHOR(S):

1. Dr. Jnaneshwara P. Shenoy
2. Dr. Shivakumar J.
3. Ms. Kanmani T.L.
4. Dr. Shailaja Moodithaya
5. Dr. Amrit Mirajkar
6. Dr. Preethi Ganapathi Pai

PARTICULARS OF CONTRIBUTORS

1. Associate Professor, Department of Physiology, Father Muller Medical College, Mangalore
2. Assistant Professor, Department of Physiology, KIMS, Hubli
3. Final year MBBS Student K S Hegde Medical Academy, Mangalore
4. Asso. Prof Department of Physiology, K S Hedge Medical Academy, Mangalore.
5. Prof & Head Department of Physiology, K S Hedge Medical Academy, Mangalore.
6. Asso. Prof, Department of Pharmacology, Kasturba Medical College, Mangalore, Manipal University

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Jnaneshwar Shenoy
Associate Professor, Department of Physiology,
Father Muller Medical College, Mangalore – 575002
Phone: +91 9886732843
E-mail: drjnani@yahoo.co.in

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